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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 03062004

Application Number: 08/854,825
Filing Date: 12 May, 1997
Appellant(s): Chisari, F., and A. Cerny

Allen Bloom (Reg. No. 29,137)
For Appellant

EXAMINER'S ANSWER

This is in response to appellants' brief on appeal filed 17 November, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellants' statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellants' statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 67-97 stand or fall together because appellants' brief does not include a clear and concise statement

that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 C.F.R. § 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal:

- Smith *et al.*, 1997, "Oncogenic mutations in ras create HLA-A2.1 binding peptides but affect their extracellular antigen processing", Intl. Immunol. 9(8):1085-1093.
- Bertoletti *et al.*, 1994, "Cytotoxic T lymphocyte response to a wild type hepatitis B virus epitope in patients chronically infected by variant viruses carrying substitutions within the epitope", J. Exp. Med. 180:933-943.
- Hahn *et al.*, 1992, "$CD8^+$ T cell recognition of an endogenously processed epitope is regulated primarily by residues within the epitope", J. Exp. Med. 176:1335-1341.
- Johnson *et al.*, 1992, "Identification of overlapping HLA class I-restricted cytotoxic T cell epitopes in a conserved region of the human immunodeficiency virus type 1 envelope glycoprotein: definition of minimum epitopes and analysis of the effects of sequence variation", J. Exp. Med. 175:961-971.
- Del Val *et al.*, 1991, "Efficient processing of an antigenic sequence for presentation by MCH class I molecules depends on its neighboring residues in the protein", Cell 66:1145-1153.
- Nayersina *et al.*, 1993, "HLA-A2 restricted cytotoxic T lymphocyte responses to multiple hepatitis B surface antigen epitopes during hepatitis B virus infection", Proc. Natl. Acad.

Sci. USA 88:10445-10449.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 67-97 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims are directed toward a large genus of peptides comprising HCV CTL epitopes carrying one to two amino acid additions, deletions, or substitutions. Immunogenic and pharmaceutical compositions comprising the claimed peptides, as well as, various methods of use are also claimed. Additional embodiments are also directed toward conjugates comprising the peptides of interest.

The written description requirement under Section 112, first paragraph, stipulates that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have decided that the specification must demonstrate that the inventor had **possession** of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, nonetheless, **the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed.** *Ralston Purina Company* v. *Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177 (C.A.F.C. 1985). *In re Wilder, et al.*, 222

U.S.P.Q. 369 (C.A.F.C. 1984). *In re Wertheim, et al.*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Blaser, Germscheid,* and *Worms,* 194 U.S.P.Q. 122 (C.C.P.A. 1977). *In re Driscoll,* 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter* v. *Hiraga,* 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California* v. *Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). *In re Bell,* 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993). *In re Deuel,* 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995). Moreover, the courts have decided repeatedly that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed chemical compound, particularly as it applied to nucleic acids and peptides (*University of California* v. *Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991); *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993); *In re Bell,* 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel,* 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). Thus, it is not sufficient to simply provide a vague reference to the biological activity of any given amino acid sequence or some generic method of obtaining it.

The skilled artisan, upon perusal of the disclosure, would **not** accept the finding that applicants were in possession of the various peptidic variants currently encompassed by the claim language. The disclosure describes the preparation of HCV CTL epitopes through a random screening process. CTL epitopes were identified in various HCV gene products. However, **there are a number of deficiencies that clearly fail to place the applicants in possession of the claimed peptidic variants. First, the**

disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating the CTL-like properties of any given peptide. The disclosure fails to identify those portions of any given peptide that are critical for the retention of HCV CTL activity. **Second, the disclosure fails to provide sufficient guidance pertaining to acceptable amino acid additions, substitutions, and deletions that will result in retention of the desired HCV CTL epitope.** Thus, it is not clear from reviewing the specification which of the many possible amino acid changes are acceptable. **Third, the prior art teaches that single amino acid changes, as well as, the addition or deletion of flanking regions, can influence the immunological properties of any given CTL epitope in an unpredictable manner** (Smith *et al.*, 1997; Bertoletti *et al.*, 1994; Johnson *et al.*, 1992; Hahn *et al.*, 1992; Del Val *et al.*, 1991; and, Eisenlohr *et al.*, 1992). Moreover, as previously noted, **the art teaches that the mere presence of an MHC class I binding motif in a peptide is not sufficient to confer binding to the appropriate class I molecule** (Nayersina *et al.*, 1993; Bertoletti *et al.*, 1994; Eisenlohr *et al.*, 1992). Finally, as previously noted, the art teaches that the capacity of a putative CTL epitope to bind to a class I molecule does not mean that the epitope will be immunogenic (Nayersina *et al.*, 1993; Eisenlohr *et al.*, 1992). The specification is silent concerning these caveats. The claims encompass a large genus of peptides that can carry substitutions, insertions, and/or deletions. The specification does not describe the synthesis, isolation, and characterization of a single mutant peptide. The specification does not teach which amino acids within any given epitope can tolerate modifications. The disclosure does not teach which amino acids can be used as replacements. Thus, **the skilled artisan would**

reasonably conclude that applicants were not in possession of the claimed invention at the time of filing and are simply attempting to capture subject matter to which they are clearly not entitled.

The previous rejection of claims 67-97 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 11-33 of U.S. Patent No. 5,709,995, is hereby withdrawn in response to the terminal disclaimer recently submitted.

(11) Response to Argument

Applicants traverse and submit that adequate written support exists for the limitations pertaining to the relative amount of sequence variability claimed. Applicants' arguments are not relevant to the rejection previously set forth under this statute. The claims were rejected under the first paragraph of 35 U.S.C. § 112 because they failed to provide a sufficient written description for the large number of peptides currently encompassed by the claim language. As previously set forth, the claims were rejected because of the following issues: 1) The disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating the CTL-like properties of any given peptide. 2) The disclosure fails to provide sufficient guidance pertaining to acceptable amino acid additions, substitutions, and deletions that will result in retention of the desired HCV CTL epitope. 3) The prior art teaches that single amino acid changes, as well as, the addition or deletion of flanking regions, can influence the immunological properties of any given CTL epitope in an unpredictable manner (Smith *et al.*, 1997; Bertoletti *et al.*, 1994; Johnson *et al.*, 1992; Hahn

et al., 1992; Del Val *et al.*, 1991; Eisenlohr *et al.*, 1992). 4) The art teaches that the mere presence of an MHC class I binding motif in a peptide is not sufficient to confer binding to the appropriate class I molecule (Nayersina *et al.*, 1993; Bertoletti *et al.*, 1994; Eisenlohr *et al.*, 1992). 5) The art teaches that the capacity of a putative CTL epitope to bind to a class I molecule does not mean that the epitope will be immunogenic (Nayersina *et al.*, 1993; Eisenlohr *et al.*, 1992). The rejection was based upon these arguments and the relevant case law, not any particular limitations pertaining to the particular degree of sequence variation claimed.

Applicants alternatively argue that a written description rejection based upon *Lilly* is also inappropriate. This rationale is clearly not supported by the law and arguments set forth *supra*. Several decisions were relied upon in determining whether or not the claim meets the appropriate requirements set forth under the statute. As previously set forth, the written description requirement under Section 112, first paragraph, stipulates that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have decided that the specification must demonstrate that the inventor had possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, nonetheless, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *Ralston Purina Company* v. *Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177 (C.A.F.C. 1985). *In re Wilder, et al.*, 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Wertheim, et al.*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Blaser, Germscheid,* and *Worms*, 194 U.S.P.Q. 122 (C.C.P.A. 1977).

In re Driscoll, 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter* v. *Hiraga*, 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993). *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995). Moreover, the courts have decided repeatedly that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed chemical compound, particularly as it applied to nucleic acids and peptides (*University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991); *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993); *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). Thus, it is not sufficient to simply provide a vague reference to the biological activity of any given amino acid sequence or some generic method of obtaining it.

In the instant application, the claims are directed toward a large genus of compounds. However, as noted in the rejection, considerable unpredictability is present in the art as it pertains to the effects of amino acid replaceability on peptide function. The disclosure merely references a large genus of compounds. However, **the specification fails to lead the skilled artisan toward any particular species**, other than the specific peptides set forth in the application. Accordingly, the rejection is hereby proper and maintained.

Respectfully submitted,

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Patent Examiner

James C. Housel
Supervisory Patent Examiner
Art Unit 1648

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Conferee

06 March, 2004